provide a tunable parameter that can be used to enhance pluripotent cell-based differentiation protocols, while also allowing for insights into the biophysical mechanisms underlying the cell fate specification and spontaneous self-organization required for coordination of embryonic development.

P2374

Board Number: B1349

The Role of Phosphatidylinositol Transfer proteins (PITPs) in Mouse Brain Development.

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Inositol (Ins) and phosphoinositide (PIP) signaling pathways are major intracellular regulatory systems of eukaryotic cells. Phosphatidylinositol transfer proteins (PITPs) execute novel modes of inositol lipid signal control by tightly channeling PIP production to specific biological outcomes. PITPα and PITPβ are highly expressed in mouse embryonic neocortex. We exploit an in utero electroporation approach to investigate the role of PITP-dependent inositol lipid signaling in the embryonic neural stem cell (NSC) pool. We found that the combination of a PITPα null mouse line and PITPβ silencing evokes a dramatic depletion of NSC pools in embryonic brain. And, we finally have generated PITPαflox/flox and PITPβflox/flox single mutants, and PITPαflox/flox,PITPβflox/flox double mutant mouse line. In an experiment using Emx1-Cre driver, which is forebrain specific driver, eviction of both PITPα and PITPβ in forebrain leads to a mouse that is born but has an amazing microcephaly that is due to virtual loss of the forebrain. Neither PITPα nor PITPβ eviction alone has any such effect. This experiment result is consistent with In utero electroporation data. Thus, we demonstrate that PITPα and PITPβ redundantly control NSC homeostasis in mouse brain development. Based on these data, we observed carefully daughter cell fate during NSC division and confirmed PITPs deficiency defeats NSC division program, asymmetric self-renewing/differentiating cell divisions. Moreover, we exploited our unique library of mutant PITPs with defined biochemical defects, to assess whether PtdCho- and PtdIns-binding are required for PITP function in embryonic NSCs. Our research will generate completely new information regarding how lipid signaling contributes to NSC homeostasis in the developing mammalian brain.

P2375

Board Number: B1350

Role of Pumilio proteins during neural crest development.

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The neural crest (NC) is a multipotent stem cell-like population, unique to vertebrates, that is characterized by its migratory behavior and broad ability to differentiate into many diverse derivatives including elements of the cardiovascular system, bone and cartilage of the face, the peripheral nervous system, and melanocytes. After neurulation, neural crest cells (NCC) delaminate, undergo EMT from the neural tube, and migrate both individually and collectively as chains. Various developmental diseases, including craniofacial abnormalities and neural crest-derived cancers such as melanoma arise due to improper development of NC. While there has been much focus on transcriptional mechanisms in regulation of neural crest specification, the process of cell migration involves rapid changes that likely require post-transcriptional regulation. In order to uncover novel proteins that might influence NC development, we have performed transcriptional profiling of migrating neural crest cells and found >300 genes that are upregulated in the migrating crest including the sequence specific RNA binding protein

Pumilio1 (PUM1). PUM proteins are evolutionarily conserved translational regulators that play essential roles during germline development in both invertebrates and vertebrates. Here, we showed that *pum1* and *pum2* mRNA is present in both premigratory and migratory NC. Pum loss of function resulted in depletion of NC cells migrating neural tube. Conversely, over expression led to an increase in numbers of migrating cells. This led us to think about the potential role of PUM proteins in modulating the specification of NC cells. To identify potential NC targets of PUM, we carried out a bioinformatics screen focusing on NC relevant genes across multiple species that possessed a Pumilio Response Element (PRE) in their 3'UTR region. The PRE element, 5'-UGUANAUA-3,' is a highly conserved consensus that PUM proteins recognize in the 3'UTRs of their targets. Interestingly, several neural crest markers possess a PRE, thus representing potential targets regulated by Pumilio during NC development. Investigation of the specific mechanism whereby PUM proteins regulate NC development is currently in progress.

P2376

Board Number: B1351

RNF220 mediated K-63 linked ubiquitinagion induces sequestration of Gli to pattern the ventral neural tube.

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The Sonic Hedgehog gradient plays crucial roles in patterning the ventral neural tube in vertebrates. In mammals, the effect of Shh signaling is mediated by the three Gli transcription factors. Gli1 works as an activator and Gli3 mostly as a repressor. The repressor and activator activities of the Glis form opposite gradients in the ventral neural tube to govern local differentiation of the neurons. However, the regulation of the Glis by factors in addition to Shh signaling itself remains to be explored. Here we identify RNF220, an ubiquitin E3 ligase, as a key regulator of ventral neural patterning through modulation of the Glis. RNF220 is specifically expressed in the ventral neural tube and knockout of RNF220 leads to ventral expansion of the medial V1 cells, dorsal expansion of the ventral V3 cells and loss of the V2 cells, suggesting increased activities of both the repressor and activator forms of the Glis. We showed that RNF220 interacts with all Glis, induces their K63-linked ubiquitination and increases their distribution in the insoluble cytoskeleton fraction. K63-linked ubiquitination of Glis promotes their interaction with HDAC6, an ubiquitin-binding and microtubule-associated deacetylase, which are then recruited to microtubules. In this way, a large fraction of Glis are sequestered from further procession or function, which greatly affects the shape of the Gli gradient. Our work revealed a novel mechanism for the shaping of gradient mediated by specific ubiquitination and sequestration.

P2377

Board Number: B1352

Satellite glial cells represent a population of arrested Schwann cell precursors.

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Satellite Glial Cells (SGCs) are cells in the peripheral nervous system that envelope the neuronal cell body and tightly regulate the neuronal microenvironment. Not much is known about the origin or fate of SGCs, but some studies have shown that these cells are able to give rise to many different cell types. Here, we examine the development of SGCs and assess their differentiation potential. We show that rat